REMARKS

I. Status of the Claims

Claims 1-4, 6, and 20-25 are under examination. Claims 1 and 20 have been amended and claims 22-23 have been cancelled.

Claim 1 has been amended to recite "wherein the antibody promotes bone-forming activity in a mammal." Claim 20 has been amended to recite that the antibody is generated using frizzled related protein-1 (sFRP-1) of SEQ ID NO:2 as an immunogen. Support for these amendments may be found throughout the specification and in particular in original claim 1, and in paragraphs 12, 41-42, 47, and 103-106 of the published application (U.S. Patent Application No. 2008/0166356-A9).

No new matter has been added. Reconsideration of the claims in view of the present amendments and remarks is respectfully requested.

II. Amendments to the Specification

The first line of the specification was previously updated to reflect that Application Serial No. 10,169,545 is now U.S. Patent No. 7,098,372. (*See* U.S. Patent Application No. 2008/0166356-A9).

III. Claim Rejections

A. Maintained Rejections under 35 U.S.C. §112, first paragraph; Enablement

Claims 20-24 remain rejected under 35 U.S.C. §112, first paragraph as allegedly lacking full enablement. In order to expedite prosecution of the present case, and without conceding the Examiner's position or the validity of the rejection, Applicant has amended claim 20 to recite "at least one antibody generated using a secreted frizzled related protein-1 (sFRP-1) of SEQ ID NO:2 as an immunogen." Claims 22-23 have been cancelled without prejudice or disclaimer.

The amended claims are fully enabled for generating an antibody using a secreted frizzled related protein-1 (sFRP-1) of SEQ ID NO:2 as an immunogen, including the specified

fragment recited in claim 24. The Examiner has acknowledged on page 3 of the Office Action, that the specification is enabling for:

> a pharmaceutical composition for regulating bone-forming activity in a mammal comprising an antibody generated using the sFRP-1 of SEQ ID NO:2, which is encoded by the polynucleotide of SEQ ID NO:1, or using the fragment of sFRP-1 of amino acids 217-231 of SEQ ID NO;2, as an immunogen, and wherein the antibody is capable of inhibiting cell death mediated by overexpression of the polynucleotide set forth in SEQ ID NO:1.

Thus, the rejections under 35 U.S.C. § 112, first paragraph, have been obviated and Applicants respectfully request that these rejections be withdrawn.

B. Rejections under 35 U.S.C. §102(e)

The rejection of claims 20-24 under 35 U.S.C. §102(e) as allegedly being anticipated by U.S. Patent No. 6,433,155 ("Umansky") has been maintained. The Examiner asserts that Umansky discloses a pharmaceutical composition comprising an antibody against a polypeptide of the SARP (secreted apoptosis related protein) family that includes murine msarp1, as well as human hsarp1, hsarp2, and hsarp3.

According to the Examiner, SARP-2 is also known as sFRP-1 and shares 99.7% similarity to the sFRP protein of SEQ ID NO:2 of the present application and exhibits 100% identity to amino acids 217-231 of SEQ ID NO:2. The Examiner concedes that Umansky does not expressly teach pharmaceutical compositions for regulating bone-forming activity in a mammal. The Examiner concludes, however, that this function would be inherent in the composition, since it allegedly has exactly the same components recited in the claims.

Anticipation requires that each and every element of the rejected claim(s) be disclosed in a single prior art reference. *See* MPEP § 2131 (8th Ed., Rev. 4, Jan. 2006). "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

In order to expedite prosecution of the present case, and without conceding the Examiner's position or the validity of the rejection, claim 20 has been amended to recite "at least one antibody generated using a secreted frizzled related protein-1 (sFRP-1) of SEQ ID NO:2 as an immunogen and wherein the antibody is capable of inhibiting cell death mediated by overexpression of the polynucleotide set forth in SEQ ID NO:1." Claims 22-23 have been cancelled. Claims 20 and 24 require that the pharmaceutical composition comprises an antibody that is capable of inhibiting cell death mediated by overexpression of the polynucleotide set forth in SEQ ID NO:1.

As an initial matter, the SARP proteins described by Umansky are not identical to the sFRP-1 protein of SEQ ID NO:2. Thus, it follows that antibodies generated using Umansky's protein or fragments thereof, will be different from the claimed antibodies. Therefore, Umansky cannot anticipate antibodies generated using an sFRP-1 protein of SEQ ID NO:2 as an immunogen. The claimed compositions and the antibodies of Umansky are not identical as concluded by the Examiner. It is noted that even though there is a region of identity between Umansky's SARP protein and SEQ ID NO:2 (i.e., amino acids 217-231) claim 24 requires that the antibody is generated using at least this fragment as an immunogen and is also capable of inhibiting cell death mediated by overexpression of the polynucleotide set forth in SEQ ID NO:1. Thus, since claims 20 and 24 require the use of a secreted frizzled related protein-1 (sFRP-1) of SEQ ID NO:2 as an immunogen, Umansky cannot anticipate the pending claims.

Furthermore, Umansky provides no teaching or suggestion with regard to the unexpected property of the claimed pharmaceutical compositions comprising the claimed antibodies for regulating bone-forming activity in a mammal. Finally, Umansky does not teach an antibody with the property that it is capable of inhibiting cell death mediated by overexpression of the polynucleotide set forth in SEQ ID NO:1.

In view of the remarks and amendments provided herein, Umansky fails to anticipate pending claims 20-21, and 24.

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The rejection of claims 20-24 under 35 U.S.C. §102(e) as allegedly being anticipated by Rubin et al. (U.S. Patent No. 6,479,255) ("Rubin") has been maintained. The Examiner states that

Rubin teaches a polypeptide, such as an antibody capable of specifically binding an FRP polypeptide. Additionally, the Examiner states that Rubin teaches an FRP amino acid sequence having 95.5% similarity to SEQ ID NO:2 of the instant application and the corresponding polynucleotide sequence with 97.4% similarity to SEQ ID NO:1 of the instant application.

The Examiner concedes that Rubin does not teach a polypeptide or polynucleotide that is identical to those of the Applicants' and also does not expressly teach pharmaceutical compositions for regulating bone-forming activity in a mammal. The Examiner concludes, however, that this function would be inherent in the composition, since it allegedly has exactly the same components recited in the claims.

Claim 20 has been amended to recite "at least one antibody generated using a secreted frizzled related protein-1 (sFRP-1) of SEQ ID NO:2 as an immunogen wherein the antibody is capable of inhibiting cell death mediated by overexpression of the polynucleotide set forth in SEQ ID NO:1." Claim 24 recites that the antibody is generated using at least a specific base fragment of sFRP-1 protein of SEQ ID NO:2 and is capable of inhibiting cell death mediated by overexpression of the polynucleotide set forth in SEQ ID NO:1. Claims 22-23 have been cancelled without prejudice or disclaimer.

As acknowledged by the Examiner, the FRP protein described by Rubin is not identical to the sFRP-1 protein of SEQ ID NO:2. Thus, since claims 20 and 24 require the use of a secreted frizzled related protein-1 (sFRP-1) of SEQ ID NO:2 as an immunogen, Rubin cannot anticipate the pending claims. Likewise, Rubin does not teach an antibody that is capable of inhibiting cell death mediated by overexpression of the polynucleotide set forth in SEQ ID NO:1. Thus, Rubin cannot anticipate the presently claimed antibodies and fails to anticipate the pending claims. Reconsideration of claims 20-21, and 24 and withdrawal of the rejections of these claims under 35 U.S.C.§ 102(e) is requested.

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Claims 1, 3-4, 6, and 20-25 have been newly rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Rubin *et al.* (US 2003/0175864 A1, with a provisional filing date of May 29, 1997) ("Rubin II"). The Examiner states that Rubin II teaches a polypeptide, such as an

antibody capable of specifically binding an FRP polypeptide. Additionally, the Examiner states that Rubin II teaches an FRP amino acid sequence having 100% similarity to SEQ ID NO:2 of the instant application.

The Examiner admits that Rubin does not teach a polynucleotide that is identical to that of SEQ ID NO:1 and also does not expressly teach pharmaceutical compositions for regulating bone-forming activity in a mammal or that the antibody is capable of inhibiting cell death mediated by overexpression of sFRP-1 gene of SEQ ID NO:1. The Examiner concludes, however, that these functions would be inherent in the composition, since it allegedly has exactly the same components recited in the claims.

It is noted that the Examiner has conceded at page 10 of the Office Action that Rubin II does not teach that the FRP protein is from human osteoblast cells.

Claim 1 has been amended to recite "wherein the antibody promotes bone-forming activity in a mammal." Claim 20 has been amended as described above. Claims 22-23 have been cancelled. As acknowledged by the Examiner, Rubin does not teach an antibody with the property of inhibiting cell death mediated by overexpression of the polynucleotide set forth in SEQ ID NO:1. Finally, Rubin does not teach a pharmaceutical composition containing such an antibody with the property of regulating bone-forming activity in a mammal. Thus, Rubin cannot anticipate the presently claimed compositions. Thus, Rubin fails to anticipate claims 1, 3-4, 6, and 20-25. Reconsideration of claims 1, 3-4, 6, and 20-21, 24-25 and withdrawal of the rejections of these claims under 35 U.S.C.§ 102(e) is requested.

C. Rejections under 35 U.S.C. §103(a)

Claim 2 has been newly rejected under 35 U.S.C. §103(a) as being unpatentable over Rubin et al. (U. S. Publication 2003/0175864) ("Rubin II") in view of Chan *et al.* (*J. Biol. Chem.*, 1992, 267(35):25202-25207) ("Chan").

The Examiner cites Rubin for its teachings relating anti-FRP antibody compositions (including agonist, antagonist, and neutralizing antibodies) and pharmaceutical uses of these compositions. The Examiner characterizes the Rubin FRP amino acid sequence as being identical

to SEQ ID NO:2 of the instant invention. The Examiner states that even though the polynucleotide sequences are not identical, the expression product is identical. The Examiner concludes that even though Rubin does not expressly teach that the FRP antibody is capable of inhibiting cell death mediated by overexpression of sFRP-1 gene, and the use of the composition for regulating bone-forming activity, that these activities would be considered inherent in the composition since it has exactly the same components recited in the claims. The Examiner further states that the preamble phrase "for regulating bone-forming activity" is not given patentable weight. The Examiner concedes that Rubin does not disclose that the FRP protein is from human osteoblast cells (claim 2).

The Examiner relies on Chan for its teachings of a mammalian homolog, *i.e.*, the rat homolog of the Drosophila *frizzled* (*fz*) gene, which is described as being widely expressed in mammalian tissues. The Examiner states that Chan teaches that the hormonal induction of Fz proteins in osteoblasts serves to promote intracellular signaling required for function responses such as increased bone resorption (citing the Abstract).

The Examiner concludes that it would have been obvious to one of ordinary skill in the art to combine the teachings of Rubin with those of Chan to use an FRP protein isolated from human osteoblast cells for generating a pharmaceutical composition comprising an antibody against sFRP-1, wherein the sFRP-1 protein is from human osteoblast cells. The Examiner concludes that one of ordinary skill in the art would have been motivated to make such an antibody because Rubin teaches that an anti-RFP antibody can be used in a pharmaceutical composition, and Chan teaches that mammalian tissues, *i.e.* rat osteoblasts, contain such proteins. (*See*, Office Action, page 7-8).

The Examiner relies on Chan for teaching FRP from human osteoblast cells. However, Chan describes rat Fz-1 and Fz-2 proteins and provides comparisons with the Drosophila protein and merely hypothesizes about the general nature of mammalian Fz proteins. Chan provides no teaching with respect to a human protein of SEQ ID NO:2 from human osteoblast cells. Thus, the Examiner's reliance on Chan is misplaced and the combination of Rubin and Chan do not teach or suggest each and every limitation of the claimed invention.

Furthermore, as discussed herein, claim 1 has been amended to recite "an antibody generated using a secreted frizzled related protein-1 (sFRP-1) of SEQ ID NO:2 as an immunogen,

wherein the antibody promotes bone-forming activity in a mammal." Dependent claim 2 further specifies that the sFRP-1 is from human osteoblast cells. Nothing in Rubin or Chan provides a teaching or motivation, much less the expectation of success for making the claimed pharmaceutical composition comprising an antibody with the property of promoting bone-forming activity in a mammal.

For a claim to be obvious under U.S. patent law, the Examiner must explain why the difference(s) between the prior art and the claimed invention would have been obvious to one of ordinary skill in the art. Additionally, the Patent Office must articulate the reason(s) why a skilled artisan "would have recognized" that the results of the prior art "were predictable" (*see* Examination Guidelines, Department of Commerce, *Federal* Register, 72(195):57529 (October 10, 2007). Nothing in Rubin's general teaching regarding an anti-RFP antibody and Chan's description of rat Fz-1 and Fz-2 proteins would lead one of ordinary skill in the art to the claimed pharmaceutical compositions.

Therefore, reconsideration of claim 2 and withdrawal of the rejection of this claim under 35 U.S.C.§ 103(a) is requested.

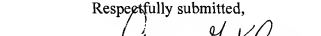
CONCLUSION

In view of the above amendments and remarks, it is respectfully requested that the application be reconsidered and that all pending claims be allowed and the case passed to issue. Applicants reserve the right to pursue the cancelled and/or non-elected subject matter in one or more continuation or divisional applications.

If there are any other issues remaining, which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Dated: July 11, 2008

Respectfully submitted,

By 

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